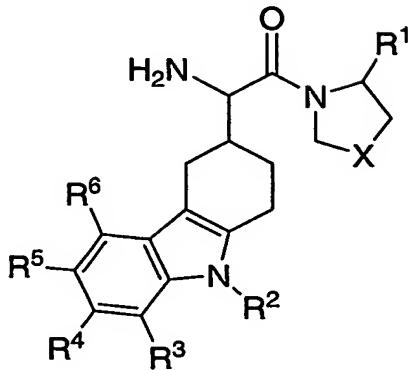


WHAT IS CLAIMED IS:

1. A compound of structural formula I:



I

5

wherein:

each n is independently 0, 1, 2, or 3;

X is selected from S, S(O), S(O)2, CH2, CHF, and CF2;

10

R1 is hydrogen or -CN;

R2 is selected from the group consisting of

hydrogen,

15 C1-6 alkyl, wherein alkyl is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, CO2H,
 C1-6 alkyloxycarbonyl, and
 (CH2)n-aryl, wherein aryl is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, CO2H,
 20 C1-6 alkyloxycarbonyl, C1-6 alkyl, C3-6 cycloalkyl, and C1-6 alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens;

R3, R4, R5, and R6 are each independently selected from the group consisting of

hydrogen,

25 halogen,
 cyano,
 hydroxy,

C₁₋₆ alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens,
C₁₋₆ alkoxy, wherein alkoxy is unsubstituted or substituted with one to five halogens,
(CH₂)_n-COOH,
(CH₂)_n-COOC₁₋₆ alkyl,
5 (CH₂)_n-CONR⁷R⁸,
(CH₂)_n-NR⁷R⁸,
(CH₂)_n-NR¹⁰SO₂R⁹,
(CH₂)_n-NR¹⁰CONR⁷R⁸,
(CH₂)_n-NR¹⁰COR¹⁰,
10 (CH₂)_n-NR¹⁰CO₂R⁹,
(CH₂)_n-aryl, wherein aryl is unsubstituted or substituted with one to five substituents
independently selected from halogen, hydroxy, CO₂H,
C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, and C₁₋₆ alkoxy, wherein alkyl and
alkoxy are unsubstituted or substituted with one to five halogens,
15 wherein any methylene (CH₂) carbon atom in R³, R⁴, R⁵, and R⁶ is unsubstituted or substituted
with one to two groups independently selected from halogen, hydroxy, and C₁₋₄ alkyl
unsubstituted or substituted with one to five halogens;

R⁷ and R⁸ are each independently selected from the group consisting of
20 hydrogen,
(CH₂)_n-phenyl,
(CH₂)_n-C₃₋₆ cycloalkyl, and
C₁₋₁₀ alkyl,
wherein alkyl is unsubstituted or substituted with one to five halogens and wherein phenyl and
25 cycloalkyl are unsubstituted or substituted with one to five substituents independently
selected from halogen, hydroxy, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy
are unsubstituted or substituted with one to five halogens; or

R⁷ and R⁸ together with the nitrogen atom to which they are attached form a heterocyclic ring selected
from azetidine, pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is
30 unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy,
C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five
halogens;

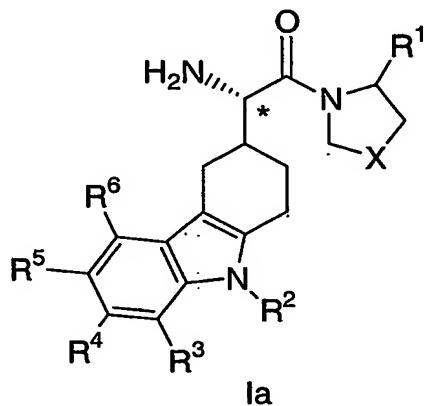
R⁹ is selected from the group consisting of (CH₂)_n-phenyl, (CH₂)_n-C₃₋₆ cycloalkyl, and C₁₋₆ alkyl,
35 wherein alkyl is unsubstituted or substituted with one to five halogens and wherein phenyl and cycloalkyl

are unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C₁-6 alkyl, and C₁-6 alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens, and wherein any methylene (CH₂) carbon atom in R⁹ is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C₁-4 alkyl unsubstituted or

5 substituted with one to five halogens; and

each R¹⁰ is hydrogen or R⁹.

2. The compound of Claim 1 of structural formula Ia wherein the carbon atom
10 marked with an * has the stereochemical configuration as depicted in formula Ia:



3. The compound of Claim 1 wherein X is S, S(O), or S(O)₂.

15

4. The compound of Claim 3 wherein R¹ is hydrogen.

5. The compound of Claim 2 wherein X is S, S(O), or S(O)₂.

20

6. The compound of Claim 1 wherein X is CH₂, CHF, or CF₂.

7. The compound of Claim 6 wherein R¹ is hydrogen.

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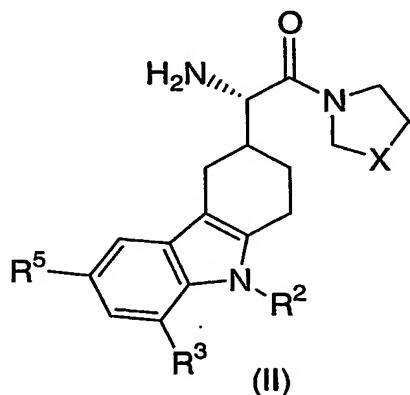
8. The compound of Claim 2 wherein X is CH₂, CHF, or CF₂.

9. The compound of Claim 1 wherein R² is hydrogen, methyl, or phenyl.

10. The compound of Claim 9 wherein R³, R⁴, R⁵ and R⁶ are each independently selected from the group consisting of hydrogen, halogen, trifluoromethyl, trifluoromethoxy, carboxy, and 5 COOC₁₋₄ alkyl.

11. The compound of Claim 10 wherein R⁴ and R⁶ are hydrogen.

12. The compound of Claim 11 of structural formula II selected from the group 10 consisting of:



<u>X</u>	<u>R²</u>	<u>R³</u>	<u>R⁵</u>
S	H	H	Cl
CH ₂	H	H	Cl
CH ₂	H	H	OCF ₃
CH ₂	H	H	CF ₃
CH ₂	H	CO ₂ H	H
CH ₂	H	CO ₂ Et	H
CH ₂	H	H	CO ₂ H
CH ₂	H	H	CO ₂ Et
CH ₂	H	CF ₃	H
CF ₂	H	CONH _n -Dec	H
CH ₂	Me	H	H
CH ₂	Ph	H	H

13. A pharmaceutical composition which comprises a compound of Claim 1 and a pharmaceutically acceptable carrier.

14. A method for treating diabetes in a mammal in need thereof which comprises the 5 administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

15. A method for treating non-insulin dependent (Type 2) diabetes in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

10 16. A method for treating hyperglycemia in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

15 17. A method for treating obesity in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

20 18. A method for treating one or more lipid disorders selected from the group of dyslipidemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, low HDL and high LDL in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

25 19. A method for treating in a mammal in need thereof one or more conditions selected from the group consisting of (1) hyperglycemia, (2) low glucose tolerance, (3) insulin resistance, (4) obesity, (5) lipid disorders, (6) dyslipidemia, (7) hyperlipidemia, (8) hypertriglyceridemia, (9) hypercholesterolemia, (10) low HDL levels, (11) high LDL levels, (12) atherosclerosis and its sequelae, (13) vascular restenosis, (14) irritable bowel syndrome, (15) inflammatory bowel disease, including Crohn's disease and ulcerative colitis, (16) other inflammatory conditions, (17) pancreatitis, (18) abdominal obesity, (19) neurodegenerative disease, (20) retinopathy, (21) nephropathy, (22) neuropathy, (23) Syndrome X, (24) ovarian hyperandrogenism (polycystic ovarian syndrome), and other disorders 30 where insulin resistance is a component, wherein the method comprises the administration to the mammal a therapeutically effective amount of a compound of Claim 1.

35 20. The pharmaceutical composition of Claim 13 further comprising one or more additional active ingredients selected from the group consisting of:

- (a) a second dipeptidyl peptidase IV inhibitor;
- (b) an insulin sensitizer selected from the group consisting of a PPAR γ agonist, a PPAR α/γ dual agonist, a PPAR α agonist, a biguanide, and a protein tyrosine phosphatase-1B inhibitor;
- 5 (c) an insulin or insulin mimetic;
- (d) a sulfonylurea or other insulin secretagogue;
- (e) an α -glucosidase inhibitor;
- (f) a glucagon receptor antagonist;
- (g) GLP-1, a GLP-1 mimetic, or a GLP-1 receptor agonist;
- 10 (h) GIP, a GIP mimetic, or a GIP receptor agonist;
- (i) PACAP, a PACAP mimetic, or a PACAP receptor agonist;
- (j) a cholesterol lowering agent such as (i) HMG-CoA reductase inhibitor, (ii) sequestrant, (iii) nicotinyl alcohol, nicotinic acid or a salt thereof, (iv) PPAR α agonist, (v) PPAR α/γ dual agonist, (vi) inhibitor of cholesterol absorption, (vii) acyl CoA:cholesterol acyltransferase inhibitor, and
- 15 (viii) anti-oxidant;
- (k) a PPAR δ agonist;
- (l) an antiobesity compound;
- (m) an ileal bile acid transporter inhibitor;
- (n) an anti-inflammatory agent; and
- 20 (o) an antihypertensive agent.

21. The pharmaceutical composition of Claim 20 wherein the PPAR α/γ dual agonist is KRP-297.

25 22. A method of treating diabetes in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of a compound of Claim 1 in combination with the PPAR α/γ dual agonist KRP-297.

30 23. A method of controlling or treating diabetes in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of a compound of Claim 1 in combination with an insulin sensitizer or an insulin secretagogue.